

The opinion in support of the decision being entered today was not written
for publication and is not binding precedent of the Board.

Paper No. 41

UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte TOSHIKAGE HIRAOKA, TETSUJI TANIMOTO,
YOSHIHIKO MAKINO, TADASHI NINOMIYA,
HIROSHI SHINOKI, YOSHIHIRO ASHIHARA,
NAOFUMI HORA, and MASASHI OGAWA

Appeal No. 2001-1657
Application No. 08/946,685

ON BRIEF

Before WINTERS, ADAMS and MILLS, Administrative Patent Judges.

MILLS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final
rejection of claims 2, 3, 5-14 and 17-28 which are the claims on appeal in this

Claim 18 is representative of the claims on appeal and reads as follows:

18. An immunoassay element for quantitatively analyzing an amount of a macromolecular antigen in a sample by determining the change in enzymatic activity of a labeling enzyme caused by a reaction between

- 1) the macromolecular antigen, and
- 2) an antibody which can react and bind specifically with the macromolecular antigen and which is labeled with the labeling enzyme;

said element comprising:

- (a) a substrate layer containing a non-diffusible substrate composed of a polymer which is capable of being digested by the labeling enzyme into a diffusible oligomer which migrates from the substrate layer; and
- (b) A reagent layer containing a digesting enzyme for further digesting the diffusible oligomer, which has migrated from said substrate layer, into a detectable monomer;

wherein the labeling enzyme is an endo-active hydrolase capable of digesting the polymer into the diffusible oligomer and the digesting enzyme is an exo-active hydrolase which digests diffusible oligomer into the detectable monomer.

The references relied upon by the examiner are:

Suda et al. (Suda)	5,093,081	March 1992
Ceska	4,066,509	Jan. 1978
Brushi	4,089,747	May 1978

(Tietz), Norbert, W., Textbook of Clinical Chemistry, pp. 729-734 (Norbert W. Tietz, ed., W.B. Saunders Company 1986)

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Grounds of Rejection

Claims 2, 3, 5-8, 12-14, 17-21 and 23-28 stand rejected under 35 U.S.C. § 103(a) as obvious over Sudo in view of Tietz and Ceska.

Claims 9-11 and 22 stand rejected under 35 U.S.C. § 103(a) as obvious over Sudo in view of Tietz and Ceska, in further view of Bruschi.

We reverse these rejections.

DISCUSSION

In reaching our decision in this appeal, we have given careful consideration to the appellants' specification and claims, to the applied prior art references, and to the respective positions articulated by the appellants and the examiner.

Rather than reiterate the conflicting viewpoints advanced by the examiner and the appellants regarding the above-noted rejection, we make reference to the Examiner's Answer for the examiner's complete reasoning in support of the rejection, and to the appellants' Brief for the appellants' arguments thereagainst. As a consequence of our review, we make the determinations which follow.

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35 U.S.C. § 103

Claims 2, 3, 5-8, 12-14, 17-21 and 23-28 stand rejected under 35 U.S.C. § 103(a) as obvious over Sudo in view of Tietz and Ceska. Claims 9-11 and 22 stand rejected under 35 U.S.C. § 103(a) as obvious over Sudo in view of Tietz and Ceska, in further view of Bruschi.

In rejecting claims under 35 U.S.C. § 103, the examiner bears the initial burden of presenting a prima facie case of obviousness. See In re Rijckaert, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993). A prima facie case of obviousness is established when the teachings from the prior art itself would appear to have suggested the claimed subject matter to a person of ordinary skill in the art. In re Bell, 991 F.2d 781, 783, 26 USPQ2d 1529, 1531 (Fed. Cir. 1993). An obviousness analysis requires that the prior art both suggest the claimed subject matter and reveal a reasonable expectation of success to one reasonably skilled in the art. In re Vaeck, 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991).

Sudo generally teaches a dry-type analytical element for immunoassays detecting analytes with a molecular weight of more than 20,000. The immunoassay element comprises a water insoluble macromolecular substrate and an enzyme conjugated antibody which reacts with the analyte in the sample, causing the enzyme to

teaches using enzymes such as amylase and cellulase in the assay because their activity can be easily measured. Answer, page 3.

The examiner indicates that Sudo differs “from the instant invention in failing to teach the use of an endo-active and an exo-active enzyme acting sequentially on the substrate to produce the detectable monomer.” Answer, page 4.

The examiner relies on Tietz for the disclosure of a chromolytic assay which uses dye labeled amylase substrate materials. Answer, page 4. Tietz teaches that a coupled enzyme assay for determining amylase activity improves the reaction stoichiometry and leads to a more controlled, and therefore, more consistent hydrolysis conditions. Tietz, pages 730-731. Tietz “teaches measuring amylase activity by te [sic] hydrolysis of starch (by the endoactive amylase) to maltose, which is hydrolyzed (by the exo-active α -glucosidase) to glucose, which is measured by a peroxidase/ABTS^[1] reaction.” Answer, page 4.

Ceska is relied on by the examiner for the disclosure of a method for detecting endo-active hydrolyzing enzymes using a dye-labeled substrate in an analytical element. The examiner submits that Ceska teaches a “water-insoluble dye-substrate composition present in a matrix layer over a carrier medium.” Answer, pages 4-5.

It is the examiner's position that (Answer, page 5):

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the analytical element and immunoassay of Sudo et al. by substituting a coupled enzyme system utilizing both the endo-active and exo-active enzyme for determining amylase activity instead of the chromolytic assay because Tietz teaches the coupled enzyme format as having many advantages over the chromolytic format, the advantages including improved reaction stoichiometry and more controlled, more consistent, hydrolysis conditions. Additionally, one would have had a reasonable expectation of success in using the coupled enzyme format of Tietz in the assay device and method Sudo et al because Ceska teaches the breakdown products of endo-active enzymes as capable of diffusing through a matrix. Therefore, one would have expected the oligomers produced by the endo-active enzyme amylase to diffuse through a matrix where an exo-active enzyme could further break them down to glucose monomers which could then be detected by the peroxidase/ABTS system of Tietz.

In response, appellants argue there is "no teaching or suggestion in Tietz that this 'coupled enzyme' assay can or should be divided into two separate reactions in spatially separated layers." Brief, page 4. Appellants further argue that, "Ceska ... teaches the detection of a single hydrolyzing enzyme in a single layer by use of a colored, immobilized polymer, and fails to provide any teachings or suggestions that would lead one of skill in the art to modify the coupled enzyme assay of Tietz to take place in two separate reactions in two separate layers." Brief, page 6. Appellants

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We agree with the appellants that the examiner has failed to present a prima facie case of obviousness. What is missing from the examiner's analysis is evidence and analysis as to why one of ordinary skill in the art would modify the coupled enzyme assay of Tietz to take place in two separate reactions in two separate layers, as argued by appellants. We do not find that Ceska, which uses a single enzyme, provides sufficient motivation to modify the coupled enzyme assay of Tietz to take place in two separate reactions in two separate layers. Nor do we find that Bruschi overcomes the deficiencies of the primary combination of references.

“In proceedings before the Patent and Trademark Office, the Examiner bears the burden of establishing a prima facie case of obviousness based upon the prior art. ‘[The Examiner] can satisfy this burden only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references.’” In re Fritch, 972 F.2d 1260, 1265, 23 USPQ2d 1780, 1783 (Fed. Cir. 1992) (citations omitted). An adequate showing of motivation to combine requires “evidence that ‘a skilled artisan, confronted with the same problems as the inventor and with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed.’” Ecolochem, Inc. v. Southern Calif. Edison Co.,

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We agree with appellants that the examiner has not met his burden of establishing a prima facie obviousness. The obviousness rejections are reversed.

CONCLUSION

The rejections of claims 2, 3, 5-8, 12-14, 17-21 and 23-28 under 35 U.S.C. § 103(a) as obvious over Sudo in view of Tietz and Ceska, and claims 9-11 and 22 under 35 U.S.C. § 103(a) as obvious over Sudo in view of Tietz and Ceska, in further view of Bruschi are reversed.

REVERSED

SHERMAN D. WINTERS
Administrative Patent Judge

DONALD E. ADAMS
Administrative Patent Judge

DEMETRA J. MILLS

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